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# *In vivo* Monitoring of Hemodynamic Changes during Clogging and Unclogging of Blood Supply for the Application of Clinical Shock Detection

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**Abstract**

This paper presents a novel methodology in early detection of clinical shock by monitoring hemodynamic changes using diffuse reflectance measurement technique. Detailed prototype of the reflectance measurement system and data analysis technique of hemodynamic monitoring was carried out in our laboratory. The real time *in-vivo* measurements were done from the index finger. This study demonstrates preliminary results of real time monitoring of reduced /- oxyhemoglobin changes during clogging and unclogging of blood flow in the finger tip. The obtained results were verified with pulse-oximeter values, connected to the tip of the same index finger.


Keywords: Clinical shock; reduced /- oxyhemoglobin; blood oxygenation; clogging; unclogging; hemodynamics

## 1. Introduction

Clinical shock is a life-threatening medical emergency and one of the most common causes of death for critically-ill patients. Clinical shock is a failure of the cardiovascular system to deliver enough oxygen and nutrients to meet cellular metabolic needs. Though the pathophysiological origins or causes of shock may vary, the end stage of all forms of shock is the same, i.e. inadequate blood flow to body tissue [1-4].

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Micro vessels are one of the key determinants of appropriate tissue perfusion during shock [5]. Currently, real time hemodynamic monitoring is a popular and reliable technique used for shock detection. The available techniques for shock detection are expensive, difficult to apply and require complex data processing. Clinical cases of shock show the same outcome at early stage that is alteration in vessel density spatial pattern and blood oxygenation changes. Therefore, mortality rates due to shock development can be reduced by monitoring these pathophysiological and hemodynamic changes at early stage and by applying appropriate medical interventions.

Tissue oxygenation is an important physiological parameter. Abnormal oxygenation of tissues and blood has been implicated in a number of diseases [6]. In addition, changes in hemodynamic parameters can provide health status information of patients. In many clinical cases due to high and low heart rate, the tissue oxygenation level is altered. In high heart rate the oxygenated blood is transported to the tissue with high pressure. As a result, the tissue does not get enough time for oxygen exchange. In such cases, the blood supply seems to be normal but tissue will not get enough oxygen for metabolism resulting in failure of vital organs. Blood is heterogeneously distributed in different tissues and tissue layers. Consequently, the optical response of tissue strongly depends on the presence of blood and its relevant parameters such as oxygen state and hematocrit [7, 8]. This opens wide possibilities for optical diagnostics because of hemoglobin concentrations. Reduced /- oxyhemoglobin concentrations and oxygen saturation provide physiologically relevant information of the tissue. Currently, pulse-oximeter [9], spectrophotometric method [10, 11], NIR [12-14] and diffuse reflectance [15-17] are used for noninvasive blood oxygenation measurement. While existing techniques do an excellent job of determining the average oxygenation state of the blood in a tissue, they cannot resolve the signal from individual vessels located within the bulk of a highly scattering tissue [11, 14]. With confocal detection Raman spectra were obtained from the blood in individual dermal microvessels, but the achievable depth is fundamentally limited to less than 100 μm due to scattering [11]. Although pulse-oximeter is widely used for blood oxygenation measurement, it has limitations such as it is not reliable when oxygen saturation is below 70 % and not very reliable when blood pressure decreases, can be affected by motion artifacts and room light variations and does not provide localized tissue oxygenation levels. Therefore, there is a need of techniques which can provide localized tissue oxygenation information.

We have proposed a novel method to detect real-time oxygenation change associated with tissue and blood vessel spatial pattern for the application of early signs of shock development. In this paper, we discuss the hemodynamic monitoring result which addresses the real time tissue hemodynamic changes. The obtained results were verified with the values obtained from a pulse-oximeter. The method of blood oxygenation monitoring associated with individual blood vessel has been previously described by the authors on a skin tissue phantom model for a macroscopic scale object [18, 19] by using spatially resolved diffuse reflectance measurement technique.

## 2. Materials and Methods

### *2.1. Experimental Methods*

The diffuse reflectance and pulse-oximeter signals were measured from the index finger of the left hand. The index finger was tied with a plastic thread near the palm to clog the blood supply to the finger. Diffuse reflectance measurements were performed by clogging and unclogging after every two minutes during the entire experiment. During clogging, the thread was slightly tightened and after two minutes signals were measured with the same procedure. The same measurement was repeated for six times. During unclogging the thread was slightly loosened and the same procedure was performed six times. The thread was tightened until the subject feels uncomfortable. Five diffuse reflectance spectra were measured

from the middle part of the finger during each interval as shown in Fig. 1. At the same time blood oxygenation values from the pulse-oximeter were measured from the tip of the same finger. The experiment was repeated three times. The experimental setup consists of a reflection-backscattering probe QR600-7-SR-125F® (Ocean Optics, USA) connected to high resolution spectrometer QE65000® (Ocean Optics, USA). A pulsed Xenon lamp PX-2® (Ocean Optics, USA) projected onto the finger *via* the reflection-backscattering probe (Ocean Optics, USA).

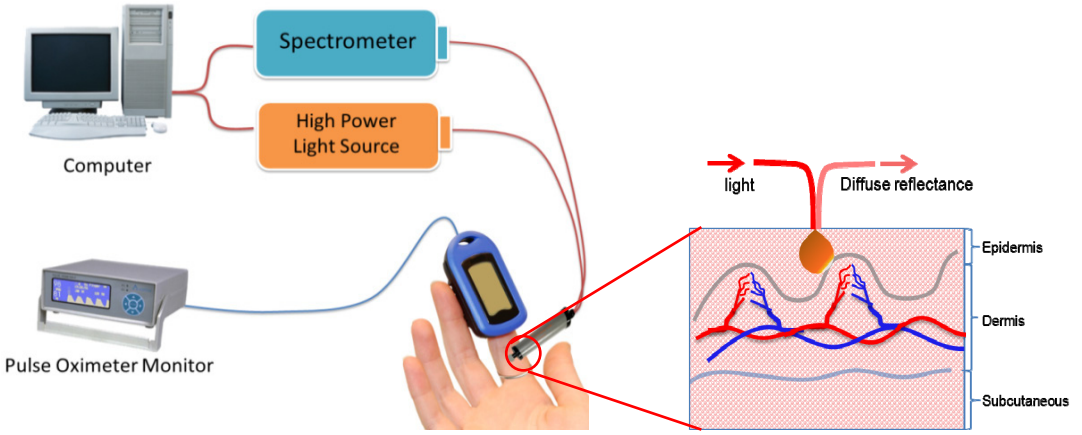


Fig. 1. Experimental setup to detect the real-time hemodynamic changes in blood oxygenation

The reflection-backscattering probe consists of a single collection fiber surrounded by six illumination fibers (NA = 0.22, d = 600 µm, multimode). The measured spectra were analyzed with a proposed mathematical model (see section 2.2) to extract the results of hemodynamic changes in reduced-hemoglobin (RHb), oxyhemoglobin ($HbO_2$) and oxygen saturation ($SO_2$) during clogging and unclogging.

### *2.2. Data analysis*

The diffuse reflectance spectrum from index finger is measured as a function of clogging and unclogging time over broad visible wavelengths ranging from λ = 298 nm to λ = 1092 nm. Three adjacent wavelengths $\lambda_0$, $\lambda_i$, $\lambda_{i+1}$ are selected to deduce equations that would allow us to retrieve the local volume fractions of RHb, $HbO_2$ and $SO_2$.

$$R(\lambda_i) = R(\lambda_0) + \frac{\partial Rd}{\partial \mu_a}\{c_{RHb}(\mu_{a,RHb}(\lambda_i) * \mu_{a,RHb}(\lambda_0)) + c_{HbO_2}(\mu_{a,HbO_2}(\lambda_i) * \mu_{a,HbO_2}(\lambda_0))\} \quad (1)$$

Where $R_d(\lambda_i)$ - diffuse reflectance measured at wavelength $\lambda_i$. RHb, $HbO_2$ - relative volume fractions of reduced and oxy-hemoglobin respectively. $\mu_{aRHb}(\lambda_i)$, $\mu_{aHbO2}(\lambda_i)$ - absorption coefficients of reduced and oxyhemoglobin at wavelength $\lambda_i$.

By simplifying the system of equations, we derived equations to calculate volume concentrations of RHb, $HbO_2$ and $SO_2$ using diffuse reflectance spectra measured at three wavelengths $R(\lambda_0)$, $R(\lambda_i)$ and $R(\lambda_{i+1})$ from the experiments. These relative local volume fractions of reduced and oxyhemoglobin concentration measured from spectra are used to detect alterations in hemodynamic changes in a localized tissue volume. The predicted hemoglobin concentrations from healthy tissue show high oxyhemoglobin concentration and less reduced-hemoglobin concentration value. Abnormal tissue state shows high reduced-hemoglobin concentration and less oxyhemoglobin concentration value.

## 3. Results and Discussion

Real-time hemodynamic changes in reduced-hemoglobin (RHb) and oxyhemoglobin concentration level during clogging and unclogging are demonstrated in Fig. 2. During clogging period the reduced-hemoglobin concentration value (showed in blue color) increases with clogging time in each step. The maximum reduced-hemoglobin concentration level is found at 12$^{th}$ minute. The insufficient supply of blood can be one of the reasons for this maximum concentration level. This maximum level was obtained during interruption of the oxygenated blood supply by pressing the palmar digital arteries which are responsible for the supply of oxygenated blood to the index finger. Therefore, during the clogging period, all the available oxygen in the local blood was consumed by the tissue, which in turn increased the reduced-hemoglobin concentration level and decreased the blood oxyhemoglobin concentration level. The reduced-hemoglobin concentration level is observed to be normal until 10$^{th}$ minute, after which it rises to maximum, this can be due to insufficient supply of blood and also due to consumption of available oxygen by the tissue. The reverse of above phenomena, i.e. the fall of reduced-hemoglobin concentration was observed during the unclogging period.

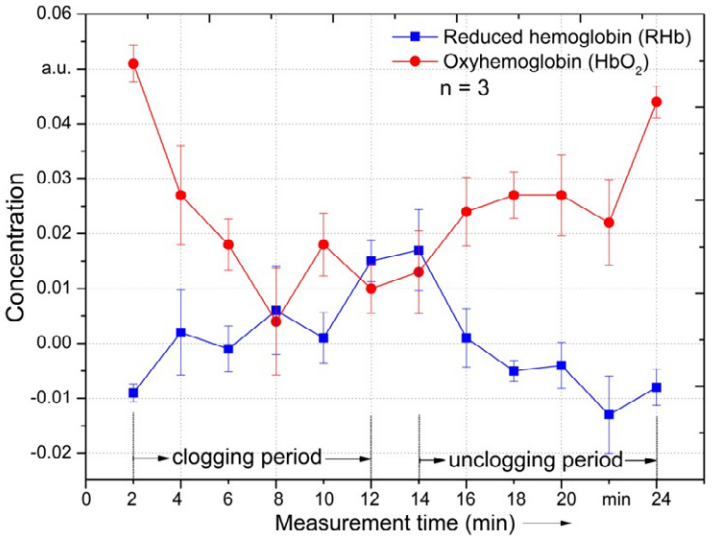


Fig. 2. Real-time reduced-hemoglobin and oxyhemoglobin changes during clogging and unclogging period measured from three experiments

The real-time hemodynamic change in oxyhemoglobin ($HbO_2$) concentration level during clogging and unclogging is shown in Fig. 2 (red color plot). The oxyhemoglobin concentration level during clogging decreased dramatically until the 8$^{th}$ minute. The interrupted supply of blood can be the reasons for this minimum concentration level. After the 8$^{th}$ minute a small increase in oxyhemoglobin concentration level is observed, this could be from outliers. Even this 8$^{th}$ minute measurement shows high error (standard deviation) value in the experimental measurement. During unclogging from 16$^{th}$ minute to 20$^{th}$ minute measurement the oxyhemoglobin concentration level was observed to be higher than the oxyhemoglobin concentration level observed during clogging period (6$^{th}$ minute to 10$^{th}$ minute). This increase in high concentration value could be from the continuous oxygenated blood supply to the local tissue and the less oxygen consumption rate of these tissues. Experimentally, lower oxyhemoglobin concentration level was observed at the end of the unclogging in comparison with the concentration level

measured at the beginning of the clogging. Fig. 2 also demonstrates the relative change in reduced-hemoglobin and oxyhemoglobin concentration level during clogging and unclogging period. These plots confirm that with increasing clogging period, the oxyhemoglobin concentration level dramatically decreases but the corresponding reduced-hemoglobin concentration level increases slowly. The reverse of above phenomena, which is dramatic decrease of reduced-hemoglobin concentration level and slow increase in oxyhemoglobin concentration level is observed during the unclogging period. The observed trends in the reduced-hemoglobin and oxyhemoglobin concentration level plot during clogging and unclogging period are almost the same.

The observed real-time hemodynamic changes in oxygen saturation ($SO_2$) level measured using our method and from pulse-oximetry both during clogging and unclogging are demonstrated in Fig 3. The change in oxygen saturation during clogging and unclogging from our method is shown in blue color plot, whereas from pulse-oximeter is shown in red color plot. During clogging the oxygen saturation level measured from our method decreases dramatically until the 8$^{th}$ minute. As light increase followed by slight decrease in oxygen saturation level was observed between the 8$^{th}$ minute and the 12$^{th}$ minute. The opposite phenomenon is measured during clogging period i.e. increase in oxygen saturation level was to be observed during the unclogging. During unclogging the oxygen saturation level increased and was observed higher than the value measured during clogging.

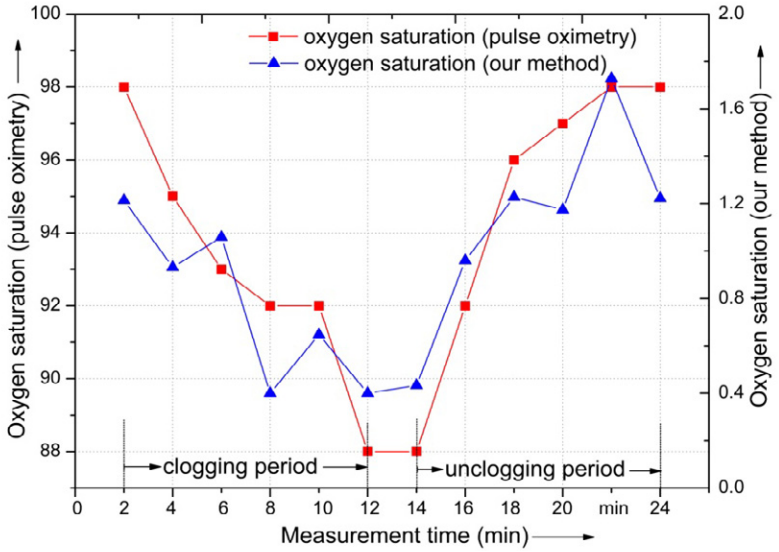


Fig. 3. The oxygen saturation measured from our method and pulse-oximeter

In the blood oxygen saturation plot obtained from the pulse-oximeter during clogging shows the oxygen saturation level decreases with time. Minimum oxygen saturation level during clogging and unclogging period is observed at the 12$^{th}$ minute. The measured trend in the blood oxygen saturation level from our method during clogging and unclogging period nearly matches with the measured trends in the blood oxygen saturation level from pulse-oximeter (Fig. 3).

High volume fraction of oxyhemoglobin and low reduced-hemoglobin associated with blood vessels or diffused blood can state the healthy state of a patient. Whereas, the low volume fractions of oxyhemoglobin, oxygen saturation and high reduced-hemoglobin predict the hypoxia or altered blood supply which could be due to clinical shock, etc. Consequently, from the rate at which oxyhemoglobin

decreases and the reduced-hemoglobin increases with time, (which could be due to the decrease in blood supply or blood pressure) one can recognize early shock symptoms promptly enough to provide a sufficient time to perform shock-preventing medical interventions. This method can be used to monitor the reconstituted blood supply in free and pedicled flap (organ implantations), blood oxygenation level during fluid replacement and assessment of hemorrhage and hemoglobin-based blood substitute resuscitation. This technique contains a bench top setup with flexible optical fiber which can be applied to any body part. It can also be used with endoscope for internal organs hemodynamic measurement.

These obtained results demonstrate that the method can monitor hemodynamic changes, which are critically important for shock detection. The altered relative local volume fractions of reduced/-oxyhemoglobin concentration can be used as a real-time and non-invasive tool for clinical monitoring and feedback of therapeutic interventions. It is necessary to validate these results with DOCT, fMRI and Raman results to confirm the accuracy of the measured blood oxygenation. In addition, it is also necessary to quantify the blood oxygenation in order to define the threshold for clinical shock. The detection procedure is rapid, simple and noninvasive, hence there are no time-consuming tests. Investigation is underway to quantify and optimize this method. In the next step we will transfer our technique to *in-vivo* animal and human tissue experiments to validate the results of this preliminary study.

## 4. Conclusions

Our preliminary result shows that the method can reasonably extract minor deviations of oxygenation and local volume blood fraction-parameters, which are directly related to the local tissue in skin or palm region. Therefore, these results are promising as the proposed method can be used to monitor the real-time hemodynamic changes non-invasively.

## Acknowledgement

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